Cardiovascular Topics

Aldosterone and renin in relation to surrogate measures of sympathetic activity: the SABPA study

Lebo F Gafane-Matemane, Johannes M van Rooyen, Rudolph Schutte, Aletta E Schutte

Abstract

Introduction: Hypertension, particularly in black populations, is often accompanied by augmented sympathetic nervous system activity and suppressed renin activity, indicative of possible blood pressure (BP) dysregulation. The potential role of the interrelationship between the renin–angiotensin–aldosterone system (RAAS) and the sympathetic nervous system in the context of low-renin conditions is unclear. We therefore explored whether surrogate measures of sympathetic activity [noradrenaline, 24-hour heart rate (HR) and percentage (%) dipping of night-time HR] relate to renin, aldosterone and aldosterone-to-renin ratio (ARR) in black and white South Africans.

Methods: We included black (n = 127) and white (n = 179) males and females aged 20–63 years. We measured 24-hour BP and HR, and calculated night-time dipping. We determined renin and aldosterone levels in plasma and calculated ARR. Noradrenaline and creatinine levels were determined in urine and the noradrenaline:creatinine ratio was calculated.

Results: More blacks had low renin levels (80.3%) compared to whites (58.7%) ($p < 0.001$). In univariate and after multivariate analyses the following significant associations were evident in only the black group: HR dipping was associated negatively with aldosterone level (β = –0.18, p = 0.024) and ARR (β = –0.20, p = 0.011), while 24-hour HR was associated positively with renin level (β = 0.20, p = 0.024). Additionally, there was a borderline significant positive association between noradrenaline:creatinine ratio and aldosterone level (β = 0.19, p = 0.051).

Conclusion: The observed associations between surrogate measures of sympathetic nervous system activity and components of the RAAS in the black group suggest that the adverse effects of aldosterone and its ratio to renin on the cardiovascular system may be coupled to the effects of the sympathetic nervous system.

Keywords: heart rate, blood pressure, dipping, renin–angiotensin–aldosterone system, noradrenaline

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Hypertension is the most common risk factor for cardiovascular events and its prevalence continues to increase in sub-Saharan Africa.[1,2] A suppressed renin–angiotensin–aldosterone system (RAAS) and increased nocturnal blood pressure (BP) (non-dipping) are among the prominent features of hypertension in black populations.[3-6] Low-renin hypertension may reflect a physiological response to increased BP and sodium/volume overload attributable to aldosterone.[7]

Even modest increases in aldosterone levels, as indicated by a high aldosterone-to-renin ratio (ARR),[8,9] particularly in the presence of high sodium intake, result in high BP in black populations.[10,11] In salt-sensitive blacks on sodium loading, blockade of angiotensin II receptors increased renin activity and reduced plasma aldosterone level, resulting in reduced night-time BP.[12] It is therefore probable that sympathetic drive and blunted decrease in aldosterone level may be the driving force for increases in night-time BP. The detrimental effects of aldosterone in black populations may be augmented by increased mineralocorticoid receptor sensitivity,[4,13] rather than increased aldosterone levels resulting from stimulation of the RAAS.

Aldosterone also influences the autonomic nervous system by, for example, blunting the baroreflex response and potentiating the vasoconstrictor effects of noradrenaline.[14,15] Blockade of aldosterone improves 24-hour heart rate (HR) variability and reduces HR, particularly in the early morning hours when sympathetic nervous system activity is high.[16] Additionally, HR is associated with muscle sympathetic nervous system activity, which is the gold standard for assessing sympathetic nervous system outflow and plasma noradrenaline levels,[17] while reduced HR dipping or a higher night-time HR can also represent a state of sympathetic nervous system overdrive.[18]

However, it is not clear if the interplay of aldosterone and its ratio to renin (ARR) with the sympathetic nervous system is evident in black populations who are predisposed to low-renin hypertension. To address this, we determined whether surrogate measures of sympathetic activity [noradrenaline, 24-hour HR and percentage (%) dipping in HR] related to renin and aldosterone levels, and ARR in black and white South Africans.

Methods

The Sympathetic activity and Ambulatory Blood Pressure in Africans (SABPA) study was conducted between February 2008 and May 2009. The study originally included 409 school teachers aged 20–65 years of age from the North West Province of South Africa.

Exclusion was based on the following criteria: ear temperature > 37.5°C, vaccinated or donated blood within three months before the study commenced, pregnancy, lactation, diabetes, any acute/chronic medication (excluding hypertension treatment) and psychotropic substance abuse or dependence.[19] For this sub-study we further excluded 62 participants on antihypertensive medication and 41 participants without renin values, with data therefore being available for 127 black and 179 white participants.

Participants were fully informed about the objectives and procedures of the study before enrolment. Assistance was given to any participant who requested conveyance of information in their home language. All participants signed an informed consent form. The study complied with all applicable requirements of the international regulations, in particular, the Helsinki Declaration of 1975 (as revised in 2008) for investigation of human participants. The Health Research Ethics Committee of North-West University (Potchefstroom campus) approved this study (NWU-00036-07-S6).

We administered validated general health and sociodemographic questionnaires, as described previously by Malan *et al.*[19] Weight, height, waist and hip circumferences were measured in triplicate by anthropometrists with calibrated instruments according to standardised methods (Precision Health Scale, A & D Co, Tokyo, Japan; Invicta Stadiometer, IP 1465, London, UK; Holtain non-stretchable metal flexible measuring tape). Body mass index (BMI) was calculated and expressed as kg/m^2.[20]

The 24-hour ambulatory BP (ABPM) and HR measurements were conducted during the working week. The ABPM apparatus (Meditech CE120® Cardiotens, Budapest, Hungary) was attached on the participant's non-dominant arm and programmed to measure BP at 30-minute intervals during the day (08:00–22:00) and every hour during the night (22:00–06:00). Percentage dipping for BP and HR, respectively were calculated for each participant as follows:

$$\% \text{ dipping BP} = \frac{\text{mean daytime BP} - \text{mean night-time BP}}{\text{mean daytime BP}} \times 100$$

$$\% \text{ dipping HR} = \frac{\text{mean daytime HR} - \text{mean night-time HR}}{\text{mean daytime HR}} \times 100$$

We therefore included 24-hour HR and its dipping as well as noradrenaline level as surrogate measures of sympathetic nervous activity.

Hypertension was defined as ABPM ≥ 130/80 mmHg, according to the European Society of Hypertension (ESH) guidelines. The validated Finometer device[21,22] (FMS, Finapres Measurement Systems, Amsterdam, Netherlands) and Beatscope® software were used to measure and calculate resting cardiac output (CO), HR and stroke volume (SV), and total peripheral resistance (TPR).

Biological sampling and biochemical analyses

Participants were requested to be in a fasted state by not eating or drinking anything except water for approximately eight to 10 hours prior to sample collection in the mornings. An eight-hour morning spot urine sample was collected, from which creatinine, sodium, potassium and noradrenaline levels were measured (Cobas Integra 400 plus, Roche, Basel, Switzerland & 3-Cat Fast Track kit, LDN, Nordhorn, Germany).

Microneurography and regional noradrenaline spill-over are the gold standards for studying sympathetic outflow[23] and were not used in this study. However noradrenaline and its metabolites are still used to assess sympathetic activity,[24] and therefore the noradrenaline:creatinine ratio was used in the present study.

Plasma noradrenaline level was not obtained in the SABPA study due to the complexity of the SABPA protocol and the short catecholamine half-life of approximately three minutes. We therefore obtained only saliva and urinary noradrenaline. In addition, using the noradrenaline:creatinine ratio instead of only urinary noradrenaline corrects/compensates for urine volume.

The blood sample was obtained with a sterile winged infusion set from the antebrachial vein branches while the participant was in a supine position for a period of 30 minutes. Samples were prepared according to appropriate methods and stored at –80°C in the laboratory.

Sequential multiple analysers (Konelab 20i, ThermoScientific, Vantaa, Finland; and Cobas Integra 400 plus, Roche, Basel, Switzerland) were used to analyse levels of total and high-density lipoprotein cholesterol (HDL-C), high-sensitivity C-reactive protein (CRP), creatinine, serum sodium, potassium, gamma-glutamyltransferase (GGT) and glycosylated haemoglobin (HbA_{1c}). Tumour necrosis factor-alpha (TNF-α) 1 was analysed with a Quantikine high-sensitivity enzyme-linked immunosorbent assay (R&D Systems, Minneapolis, MN USA). Serum cotinine was analysed with a homogeneous immunoassay (Automised Modular, Roche, Basel, Switzerland).

The modification of diet in renal disease (MDRD) formula was used to estimate glomerular filtration rate (eGFR) as a measure of renal function (serum creatinine was used in the formula). We analysed active plasma renin using the high-sensitivity radio-immunometric assay (Renin III Generation, CIS Biointernational, Cedex, France) with cross-reaction with prorenin being 0.4%. The source of reagents was mouse anti-human-active renin monoclonal antibody (IBL Lab, 38T501, USA).

Plasma aldosterone was analysed using a competitive radio-immunoassay (Beckman Coulter, Brea, CA). We used the age-specific expected normal reference values (20–40 years, mean 8.11 pg/ml, SD 3.66; 40–60 years, mean 6.18 pg/ml, SD 3.42) from the renin III CISBIO kit to divide our study population into low- and high-renin groups (Renin III Generation, CIS Biointernational, Cedex, France). The mean age for this study population was 44.4 years (SD 9.60). We therefore used 6.18 pg/ml as a cut-off value to determine the number of participants with low versus high renin levels.

Statistical analysis

We used Statistica Version 12 for all statistical analyses (Statsoft Inc, Tulsa, OK). Data were categorised and analysed according to black and white ethnicity, based on the interaction with ethnicity on the association between 24-hour HR and renin activity (β = –0.56, p = 0.019). No gender interactions were observed. The distribution of renin, aldosterone, ARR, HbA_{1c}, GGT, cotinine, total cholesterol, HDL-C, CRP, creatinine and noradrenaline were normalised by logarithmic transformation. The central tendency and spread of these variables were represented by the geometric mean and the 5th and 95th percentile intervals.

Means and proportions were compared using independent t-tests and chi-squared tests, respectively. We performed single, partial and forward stepwise multiple regression analyses to investigate associations between relevant cardiovascular variables and renin, aldosterone and ARR, as well as between aldosterone and noradrenaline:creatinine ratio. In partial regression analyses we adjusted for age, body mass index (BMI) and gender. Covariates included in the models were age, waist-to-hip ratio, gender, GGT, cotinine, urinary Na^+:K^+ ratio, total cholesterol:HDL-C ratio, HbA_{1c}, TNF-α, eGFR and TPR.

Results

Table 1 compares the black and white groups in which the frequency of low renin level was higher in the black group compared to whites (80.3% vs 58.7%, p < 0.001).The ethnic groups had similar mean ages (p = 0.35) and gender distribution (p = 0.78). Twenty-four-hour, day- and night-time systolic BP (SBP) and diastolic BP (DBP) as well as HR were higher in the black group (all p < 0.001), while percentage dipping in SBP, DBP or HR was lower in the black group compared to the white group (all p ≤ 0.042). Aldosterone (p = 0.015) and noradrenaline:creatinine ratio (p =0.044) were higher in the white group compared to the black group, while blacks had lower renin level (p < 0.001) and a higher ARR (p = 0.007) compared to whites.

We performed Pearson and partial correlations (adjusting for age, gender and BMI) to investigate the associations of surrogate measures of sympathetic activity (noradrenaline:creatinine ratio, 24-hour HR and night-time dipping in HR) with renin, aldosterone and ARR (Fig. 1, Tables 2, 3). In blacks, before and after full adjustment in multiple regression analysis, 24-hour HR associated positively with renin (β = 0.20, p = 0.024), while night-time dipping in HR associated negatively with aldosterone (β = –0.18, p = 0.024) and ARR (β = –0.20, p = 0.011) (Table 4).

Percentage dipping in SBP was positively associated with aldosterone (β = 0.23, p = 0.008) and ARR (β = 0.18, p = 0.038), while dipping in DBP was positively associated with aldosterone level (β = 0.24, p = 0.007) (Table 4). In whites, the renin level was positively associated with dipping in DBP (β = 0.16, p = 0.033) (Table 4).

Table 5 indicates the following associations in the black group: 24-hour SBP (β = –0.22, p = 0.006) and 24-hour DBP (β = –0.20, p = 0.009) associated negatively with renin level. There was also a borderline significant association of noradrenaline:creatinine ratio with aldosterone (β = 0.19, p = 0.051) (Table 5). In the white group, 24-hour SBP (β = –0.15, p = 0.021) and 24-hour DBP (β = –0.16, p = 0.019) associated negatively with renin level (Table 5).

Table 1. Comparison between black and white groups

Variables	*Blacks* (n = *127*)	*Whites* (n = *179*)	p-*value*
Age (years)	43.0 ± 7.33	44.0 ± 10.8	0.35
Women, *n* (%)	64 (50.4)	93 (52.0)	0.78
Hypertensive, *n* (%)	77 (60.6)	66 (36.9)	< **0.001**
Anthropometric measurements			
Body mass index (kg/m²)	30.2 ± 7.26	27.5 ± 6.01	**0.001**
Waist-to-hip ratio	0.87 ± 0.11	0.87 ± 0.10	0.51
Resting cardiovascular measurements[a]			
Cardiac output (l/min)	6.72 ± 1.88	6.44 ± 1.94	0.21
Heart rate (bpm)	67.9 ± 10.3	66.3 ± 10.7	0.17
Stroke volume (ml)	100 ± 27.2	97.9 ± 24.5	0.43
Total peripheral resistance (mmHg/ml/s)	1.03 ± 0.42	1.03 ± 0.53	0.93
Systolic BP			
24-hour (mmHg)	132 ± 15.4	124 ± 11.9	< **0.001**
Daytime (mmHg)	137 ± 15.4	129 ± 11.8	< **0.001**
Night-time (mmHg)	123 ± 16.1	113 ± 13.8	< **0.001**
Diastolic BP			
24-hour (mmHg)	82.5 ± 10.5	73.8 ± 9.94	< **0.001**
Daytime (mmHg)	87.7 ± 11.4	81.4 ± 8.70	< **0.001**
Night-time (mmHg)	73.4 ± 11.7	66.4 ± 9.01	< **0.001**
Heart rate			
24-hour (bpm)	79.3 ± 9.70	73.7 ± 10.2	< **0.001**
Daytime (bpm)	84.2 ± 10.4	78.7 ± 10.7	< **0.001**
Night-time (bpm)	71.0 ± 12.0	64.9± 10.3	< **0.001**
% Dipping			
Systolic BP (mmHg)	10.1 ± 6.34	12.2 ± 6.33	**0.003**
Diastolic BP (mmHg)	15.9 ± 11.9	18.2 ± 7.90	**0.042**
Heart rate (bpm)	14.6 ± 8.78	17.2 ± 9.25	**0.015**
Biochemical measurements			
Aldosterone (pg/ml)	43.7 (10.5; 170)	55.0 (21.8; 219)	**0.015**
Renin (pg/ml)	3.47 (0.95; 9.33)	5.75 (2.24; 12.3)	< **0.001**
Low renin status, *n* (%)	102 (80.3)	105 (58.7)	< **0.001**
Aldosterone-to-renin ratio	12.5 (2.95; 67.6)	9.55 (2.88; 33.1)	**0.007**
Glycosylated haemoglobin (%)	6.03 (5.25; 8.71)	5.50 (5.01; 6.31)	< **0.001**
Total cholesterol:HDL-C	4.07 (2.29; 7.41)	4.68 (2.82; 7.94)	**0.0002**
C-reactive protein (mg/l)	3.80 (0.28; 26.3)	2.04 (0.99; 8.91)	< **0.001**
Cotinine (ng/ml)	2.75 (1.00; 148)	1.86 (1.00; 209)	**0.043**
Gamma-glutamyltransferase (U/l)	43.6 (20.4; 138)	18.6 (7.08; 74.1)	< **0.001**
Tumour necrosis factor-α (IU/ml)	3.00 ± 2.13	1.90 ± 2.00	< **0.001**
Estimated glomerular filtration rate (ml/min/1.73 m²)	114 ± 27.8	94.5 ± 17.1	< **0.001**
Urinary Na^+:K^+ ratio	5.47 ± 4.11	4.09 ± 2.73	**0.0004**
Urinary noradrenaline:creatinine ratio	1.45 (0.95; 2.51)	1.55 (0.85; 2.69)	**0.044**
Lifestyle factors			
Self-reported smoking, *n* (%)	22 (17.3)	26 (14.6)	0.52
Self-reported alcohol use, *n* (%)	29 (22.8)	91 (51.1)	< **0.001**

[a]Obtained from the Finometer device. Values are arithmetic mean ± standard deviation; geometric mean (5th and 95th percentile interval) for logarithmically transformed variables. BP, blood pressure; HDL-C, high-density lipoprotein cholesterol. Bold text indicates p < 0.05.

Discussion

The main finding of this study is that in the black group, which consisted mainly of participants with low renin levels, 24-hour HR and its dipping as surrogate measures of sympathetic nervous system activity related independently and adversely to renin, aldosterone and ARR. Furthermore, there was a tendency towards a positive association between aldosterone and noradrenaline levels (p = 0.051). Previous observations in the SABPA cohort indicated a blunted baroreceptor sensitivity and

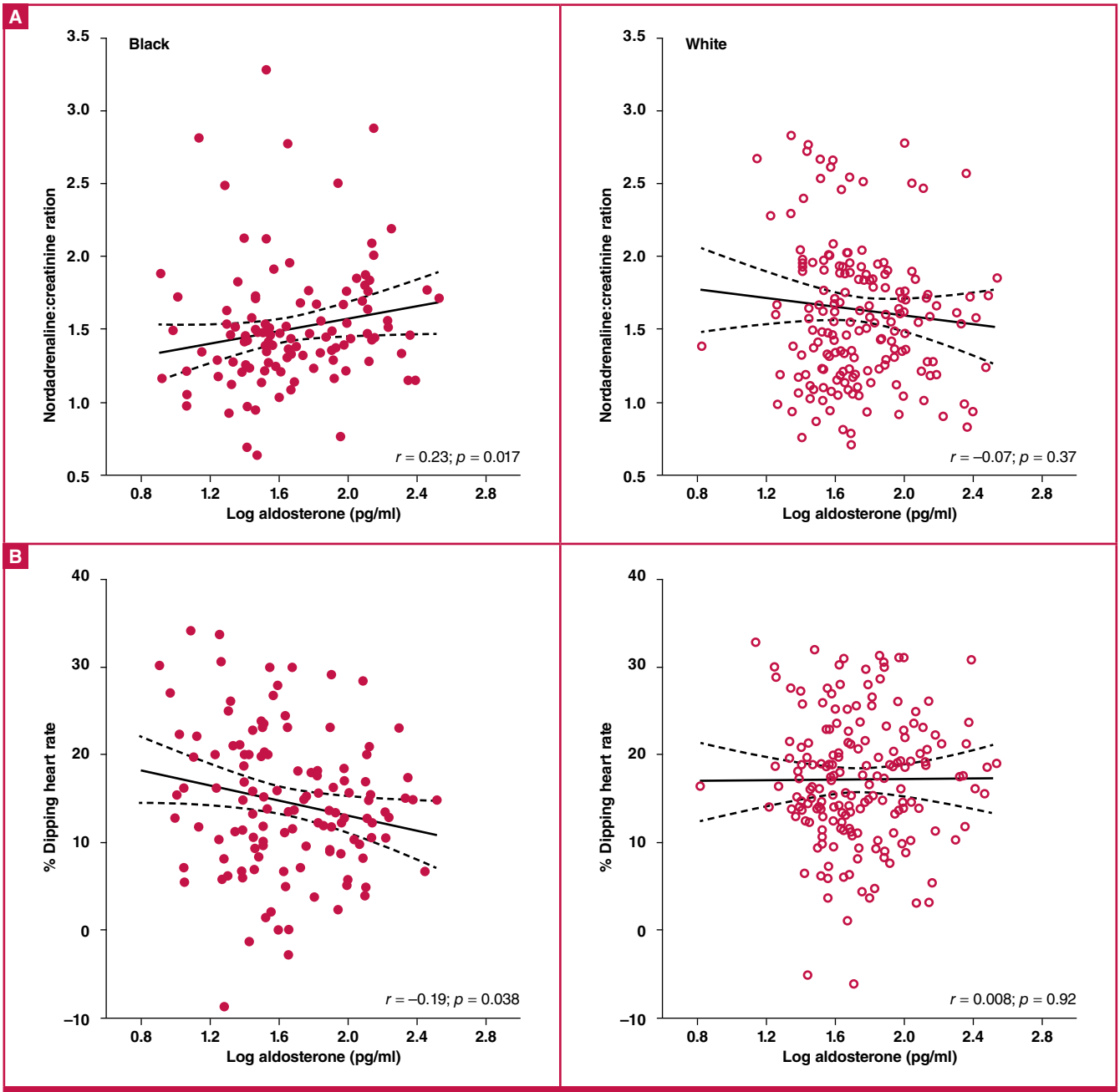

Fig. 1. Associations between (A) log noradrenaline:creatinine ratio and log aldosterone; (B) night-time dipping in heart rate and aldosterone level in black and white groups. Solid and dashed lines represent the regression line and 95% CI boundaries, respectively.

depressed HR variability, supporting the possibility of higher sympathetic activity in this population group.[25,26]

A novel finding of this study was that despite higher aldosterone levels in whites compared to blacks, aldosterone and its ratio to renin were associated with less dipping of night-time HR in blacks only. A higher HR is associated with total mortality rate, and night-time HR predicts cardiovascular mortality rate in the general population.[27] In blacks, a more pronounced sympathetic drive, as shown by an exaggerated cardiovascular reactivity to stress compared to whites, contributed to elevation of BP through increased TPR and HR.[28] The positive association between 24-hour HR and renin level may indicate β-adrenergic receptor stimulation at both the heart and kidney, resulting in increases in HR and renin secretion at the juxtaglomerular apparatus, respectively.[29] Previous findings in the same population under study indicated that even at suppressed renin levels, sympathetic stimulation by exposure to an acute stressor resulted in a positive association between TPR reactivity and renin reactivity in blacks, but not in whites.[30]

The observed association of aldosterone and ARR with attenuated HR dipping may not only be an indication of possible synergy between aldosterone and sympathetic drive, but also the direct effects of aldosterone on the cardiovascular system via high-density mineralocorticoid receptors.[31,32] The increased aldosterone sensitivity in blacks[13] may also explain the observed negative association with HR dipping, despite having lower mean aldosterone levels compared to whites.

Table 2. Pearson and partial correlations of BP, HR and noradrenaline with renin, aldosterone and ARR in black and white groups

Pearson correlations	*Blacks* (n = 127)							
	24-hour SBP		*24-hour DBP*		*24-hour HR*		*NA:creatinine ratio*	
Variables	r	p	r	p	r	p	r	p
Log renin	**–0.18**	**0.039**	**–0.18**	**0.039**	**0.24**	**0.006**	0.07	0.44
Log aldosterone	0.05	0.55	0.07	0.43	0.14	0.11	**0.23**	**0.017**
Log ARR	**0.17**	**0.052**	**0.18**	**0.034**	–0.04	0.64	0.14	0.12
	Whites (n = 179)							
	24-hour SBP		*24-hour DBP*		*24-hour HR*		*NA:creatinine ratio*	
	r	p	r	p	r	p	r	p
Log renin	–0.05	0.51	–0.07	0.34	0.06	0.41	–0.06	0.44
Log aldosterone	–0.05	0.53	–0.02	0.82	0.12	0.12	–0.07	0.37
Log ARR	–0.01	0.92	–0.01	0.92	0.06	0.41	–0.02	0.81
Adjusted for age, gender and BMI	*Blacks* (n = 127)							
	24-h SBP		*24-h DBP*		*24-h HR*		*NA:creatinine ratio*	
	r	p	r	p	r	p	r	p
Log renin	**–0.23**	**0.011**	**–0.25**	**0.005**	**0.26**	**0.004**	0.08	0.42
Log aldosterone	–0.04	0.64	–0.02	0.82	0.14	0.13	**0.22**	**0.022**
Log ARR	0.12	0.18	0.16	0.084	–0.06	0.50	0.14	0.15
	Whites (n = 179)							
	24-h SBP		*24-h DBP*		*24-h HR*		*NA:creatinine ratio*	
	r	p	r	p	r	p	r	p
Log renin	**–0.15**	**0.042**	–0.15	0.034	0.07	0.37	0.09	0.23
Log aldosterone	–0.08	0.27	–0.03	0.70	0.10	0.21	–0.04	0.093
Log ARR	0.03	0.65	0.09	0.24	0.04	0.61	–0.11	0.17

SBP, systolic blood pressure; DBP, diastolic blood pressure, HR, heart rate; NA, noradrenaline; ARR, aldosterone-to-renin ratio; BMI, body mass index. Bold text indicates $p < 0.05$.

Table 3. Pearson and partial correlations of percentage dipping in night-time BP and HR with renin, aldosterone and ARR in black and white groups

Pearson correlations	*Blacks* (n = 127)					
	% SBP		*% DBP*		*% HR*	
Variables	r	p	r	p	r	p
Log renin	0.05	0.59	0.03	0.72	0.13	0.14
Log aldosterone	**0.23**	**0.010**	**0.28**	**0.002**	**–0.19**	**0.038**
Log ARR	0.16	0.065	**0.22**	**0.013**	**–0.25**	**0.004**
	Whites (n = 179)					
	% SBP		*% DBP*		*% HR*	
	r	p	r	p	r	p
Log renin	0.13	0.091	**0.19**	**0.009**	0.12	0.11
Log aldosterone	0.07	0.39	0.09	0.22	0.001	0.92
Log ARR	–0.03	0.64	–0.06	0.42	–0.08	0.26
Adjusted for age, gender and BMI	*Blacks* (n = 127)					
	% SBP		*% DBP*		*% HR*	
	r	p	r	p	r	p
Log renin	0.06	0.51	0.05	0.61	0.11	0.24
Log aldosterone	**0.26**	**0.004**	**0.31**	**< 0.001**	**–0.19**	**0.025**
Log ARR	0.19	0.23	**0.24**	**0.008**	**–0.25**	**0.006**
	Whites (n = 179)					
	% SBP		*% DBP*		*% HR*	
	r	p	r	p	r	p
Log renin	0.14	0.062	**–0.17**	**0.021**	0.10	0.19
Log aldosterone	0.08	0.28	0.09	0.24	0.001	0.99
Log ARR	–0.03	0.72	–0.05	0.55	–0.07	0.34

SBP, systolic blood pressure; DBP, diastolic blood pressure, HR, heart rate; ARR, aldosterone-to-renin ratio; BMI, body mass index. Bold text indicates $p < 0.05$.

In the present study we also found blacks to have lower noradrenaline levels, which showed a borderline significant relationship with aldosterone. Experimental studies indicated that aldosterone prevents extraneuronal and myocardial uptake of noradrenaline and therefore may enhance its effects,[15,33] albeit at lower levels.

The higher frequency of low renin and aldosterone levels in blacks compared to whites is consistent with previous studies.[34,35] However, blacks exhibited a higher ARR. A relatively higher aldosterone level for a given level of plasma renin points to the possibility of excess aldosterone secretion, which has a significant role in salt/volume-related hypertension.[36-38] Higher ARR has been linked to a non-dipping pattern of BP in the presence of high dietary sodium levels in the general Japanese population.[39]

In our study, we showed that aldosterone and its ratio to renin were associated with an increase in BP dipping and a decrease in HR dipping. The favourable association of aldosterone and ARR with BP dipping may possibly be as a result of a compensatory mechanism for the reduced dipping in HR to maintain haemodynamic balance.

Our study should be interpreted within the context of its strengths and limitations. We did not collect 24-hour urine in order to assess noradrenaline level, and we did not assess salt intake, salt sensitivity or angiotensin II levels. Even though the use of catecholamines is not regarded as the gold standard, catecholamines and their metabolites are still used to assess sympathetic activity[24] and therefore the noradrenaline:creatinine ratio was used in our study. This was a cross-sectional study therefore causality could not

Table 4. Independent associations of 24-hour HR, night-time dipping in HR and BP with renin, aldosterone and ARR in black and white groups

	Blacks (n = 127)					
	24-h HR			*% HR*		
	Adjusted R^2	*β (95% CI)*	*p-value*	*Adjusted R^2*	*β (95% CI)*	*p-value*
Log renin	0.15	0.20 (0.93; 12.1)	**0.024**	0.19	–	–
Log aldosterone	0.13	0.09 (–2.12; 6.66)	0.31	0.29	–0.18 (–7.83; –0.61)	**0.024**
Log ARR	0.13	–	–	0.30	–0.20 (–7.28; –0.99)	**0.011**
	% SBP			*% DBP*		
	Adjusted R^2	*β (95% CI)*	*p-value*	*Adjusted R^2*	*β (95% CI)*	*p-value*
Log renin	0.10	–	–	0.12	0.10 (–2.91; 11.2)	0.25
Log aldosterone	0.14	0.23 (1.07; 6.73)	**0.008**	0.16	0.24 (2.14; 12.8)	**0.007**
Log ARR	0.12	0.18 (0.18; 5.23)	**0.038**	0.12	0.15 (0.83; 8.95)	0.11
	Whites (n = 179)					
	24-h HR			*% HR*		
	Adjusted R^2	*β (95% CI)*	*p-value*	*Adjusted R^2*	*β (95% CI)*	*p-value*
Log renin	0.22	–	–	0.13	0.10 (–1.62; 9.42)	0.17
Log aldosterone	0.22	–	–	0.13	–	–
Log ARR	0.22	–	–	0.13	–0.09 (–6.63; 1.67)	0.24
	% SBP			*% DBP*		
	Adjusted R^2	*β (95% CI)*	*p-value*	*Adjusted R^2*	*β (95% CI)*	*p-value*
Log renin	0.01	0.12 (–0.54; 7.27)	0.09	0.06	0.16 (0.46; 10.3)	**0.033**
Log aldosterone	0.0001	–	–	0.05	0.08 (–1.36; 6.48)	0.20
Log ARR	0.0001	–	–	0.04	–	–

–, log renin, log aldosterone and log ARR did not enter the forward stepwise model. Independent variables included in the model: age, waist-to-hip ratio, gender, gamma-glutamyltransferase, cotinine, urinary Na^+:K^+ ratio; total cholesterol:high-density lipoprotein cholesterol ratio, glycosylated haemoglobin, tumour necrosis factor-α, estimated glomerular filtration rate and total peripheral resistance. Associations with % dipping variables were additionally adjusted for daytime measurements. ARR, aldosterone-to-renin ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate. Values in bold indicate $p < 0.05$.

Table 5. Independent associations of 24-hour BP and noradrenaline:creatinine ratio with renin, aldosterone and ARR in black and white groups

	Blacks (n = *127*)								
	24-h SBP			*24-h DBP*			*Log noradrenaline:creatinine ratio*		
Independent variables	*Adjusted* R^2	β *(95% CI)*	p-*value*	*Adjusted* R^2	β *(95% CI)*	p-*value*	*Adjusted* R^2	β *(95% CI)*	p-*value*
Log renin	0.31	–0.22 (–19.3; –3.44)	0.006	0.37	–0.20 (–12.4; –1.88)	0.009	0.10	–	–
Log aldosterone	0.28	–	–	0.34	–	–	0.12	0.19 (0.0005 ; 0.16)	0.051
Log ARR	0.28	0.11 (–1.59; 9.53)	0.16	0.35	0.14 (–0.23; 6.89)	0.070	0.10	0.10 (–0.03 ; 0.10)	0.31
	Whites (n = *179*)								
	24-h SBP			*24-h DBP*			*Log noradrenaline:creatinine ratio*		
	Adjusted R^2	β *(95% CI)*	p-*value*	*Adjusted* R^2	β *(95% CI)*	p-*value*	*Adjusted* R^2	β *(95% CI)*	p-*value*
Log renin	**0.29**	**–0.15 (–13.9; –1.20)**	**0.021**	**0.28**	**–0.16 (–9.71; –0.93)**	**0.019**	0.34	0.08 (–0.03; 0.13)	0.22
Log aldosterone	0.28	–0.11 (–9.52; 0.96)	0.11	0.27	–0.07 (–5.61; 1.69)	0.29	0.34	–	–
Log ARR	0.27	–	–	0.26	–	–	0.34	–0.09 (–0.10 ; 0.02)	0.16

–, log renin, log aldosterone and log ARR did not enter the forward stepwise model. Independent variables included in the model: age, waist-to-hip ratio, gender, gamma-glutamyltransferase, cotinine, urinary Na^+:K^+ ratio; total cholesterol: high-density lipoprotein cholesterol ratio, glycosylated haemoglobin, tumour necrosis factor-α, estimated glomerular filtration rate, total peripheral resistance. ARR, aldosterone-to-renin ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure. Values in bold indicate $p < 0.05$.

be inferred. This homogenous sample cannot be regarded as representative of the general South African population.

Conclusion

We found in blacks only that aldosterone level and its ratio to renin was associated with less dipping in night-time HR. Our findings suggest that low-renin hypertension in black populations may be partly mediated by the direct effects of aldosterone and its relationship with the sympathetic nervous system.

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